

DB=PGPB; PLUR=YES; OP=ADJ

L11 (fish adj oil) same (antibod\$ or immunoglobulin\$ or immunosuppressive\$ or rapamycin\$)

417 L11

DB=DWPI; PLUR=YES; OP=ADJ

L10 ("DE 3781686G")!.ABPN1,NRPN.) .p22-p52.

1 L10

DB=EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ

L9 (fish adj oil) same (antibod\$ or immunoglobulin\$ or immunosuppressive\$ or rapamycin\$)

4 L9

DB=USPT; PLUR=YES; OP=ADJ

L8 L7 same (antibod\$ or immunoglobulin\$ or immunosuppressive\$ or rapamycin\$)

30 L8

L7 (fish adj oil) same (pharmaceutical or therapeutic) same (composition\$)

100 L7

L6 (rapamycin\$) and (kit\$) same (pharmaceutical or therap\$ or treat\$) same (immunosuppressiv\$)

22 L6

L5 (rapamycin\$) and (kit\$) same (pharmaceutical or therap\$ or treat\$) same (antibod\$)

115 L5

L4 (rapamycin\$) and (kit\$) same (pharmaceutical or therap\$ or treat\$)

516 L4

DB=PGPB; PLUR=YES; OP=ADJ

L3 11

51 L3

DB=USPT,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ

L2 L1

25 L2

DB=PGPB,USPT,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ

L1 (rapamycin\$) same (kit\$) same (pharmaceutical or therap\$ or treat\$)

76 L1

END OF SEARCH HISTORY



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(54) METHODS OF INHIBITING T CELL PROLIFERATION OR IL-2 ACCUMULATION WITH CTLA-4 SPECIFIC ANTIBODIES

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(57) ABSTRACT

Isolated ligands which bind a molecule expressed on the surface of T cells and induce antigen specific apoptosis in activated T cells are disclosed. Preferably, the T cell surface molecule is CTLA4 and the ligand is a monoclonal anti-CTLA4 antibody that binds to an epitope of CTLA4 distinct from the binding sites of B7-1 and B7-2. Upon binding of the antibody to CTLA4 on an activated T cell, in the presence of an antigenic signal, antigen specific apoptosis is induced. The invention also describes a novel natural CTLA4 ligand, distinct from B7-1 and B7-2, which mediates induction of apoptosis. Pharmaceutical compositions of anti-CTLA4 antibodies or other isolated CTLA4 ligands which can be administered to subjects to induce T cell apoptosis, thereby clonally deleting antigen specific T cells, such as alloreactive T cells in transplantation situations or autoreactive T cells in autoimmune disorders, are also disclosed. Methods for inducing T cell apoptosis in vitro with an anti-CTLA4 antibody or other ligand of the invention together with an antigen specific signal are also disclosed, e.g., for use in purging alloreactive T cells from donor bone marrow prior to bone marrow transplantation to inhibit graft versus host disease.

